Group III	Corresponding claims 1, 4, 11, 14, and 17-24 drawn to a protein constituting a mammalian neuronal cationic channel represented in SEQ ID NO 3.
Group IV	Corresponding claims 1, 5, 11, 15, and 17-24 drawn to a protein constituting a mammalian neuronal cationic channel represented in SEQ ID NO 4.
Group V	Corresponding claims 1, 6, 11, 16, and 17-24 drawn to a protein constituting a mammalian neuronal cationic channel represented in SEQ ID NO 5.
Group VI	Corresponding claims 7-9, 11, 12, and 17-24 drawn to hybrid cationic channels containing SEQ ID NO 1.
Group VII	Corresponding claims 7-9, 11, 13, and 17-24 drawn to hybrid cationic channels containing SEQ ID NO 2.
Group VIII	Corresponding claims 7-9, 11, 14, and 17-24 drawn to hybrid cationic channels containing SEQ ID NO 3.
Group IX	Corresponding claims 7-9, 11, 15, and 17-24 drawn to hybrid cationic channels containing SEQ ID NO 4.
Group X	Corresponding claims 7-9, 11, 16, and 17-24 drawn to hybrid cationic channels containing SEQ ID NO 5.
Group XI	Corresponding claims 10 and 24 drawn to an antibody.
Group XII	Corresponding claim 25 drawn to a use of a chemical or biological substance that is capable of modifying the currents of an ionic channel.

This requirement is respectfully traversed. As the Examiner is aware, a restriction requirement in this case must comply with PCT Rule 13.1 and 37 CFR §1.475 because this application was filed as the national stage application of a PCT patent application. Accordingly, the standard for restriction is unity of invention. Unity of invention is present when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. Special technical features are those technical features that define a contribution which the invention makes over the prior art. Applicants contend that the groups of claims in the present case define a single invention with shared special technical features.

The Examiner has found that Group I does not share special technical features with the other groups. Applicants respectfully traverse. However, Applicants also point out that MPEP § 1850 expressly states that, "The Commissioner has decided *sua sponte* to partially waive 37 CFR 1.475 and 1.499 et seq. to permit applicants to claim up to ten (10) nucleotide sequences that do not have the same or corresponding special technical features without the payment of an additional fee." While this pertains specifically to PCT practice, 37 CFR §1.475 expressly makes these rules applicable in this case. The first ten groups enumerated by the examiner have been separated on the basis of different nucleotide sequences. In accordance with MPEP §1850, these groups should be combined into one. If the groups are so combined, Applicant would elect this group.

Applicants reiterate the following remarks regarding shared special technical features. The invention is directed to the ASIC family of proton activated, amiloride-sensitive mammalian neuronal cationic channels. The molecular sequence of the human ASIC1 channel is shown in SEQ ID NO:2. The molecular sequence of the human ASIC2 is represented by the human

MDEG channel and is shown in SEQ ID NO:3 and SEQ ID NO:6. The corresponding rat ASIC1 channel is shown by SEQ ID NO:1 and SEQ ID NO:4. The rat ASIC3, represented by rat DRASIC channel, is shown in SEQ ID NO:5. These are highly conserved sequences. For example the rat and human ASIC2 channels are 99% identical.

All of the channels claimed in the Application are activated by protons. Furthermore, all of the channels claimed in the Application are amiloride-sensitive. These special technical features, proton activation and amiloride sensitivity, are shared among the ASIC family, and these isolated ASIC family members represent an advance over the prior art.

We respectfully submit that the high homology between the members of the ASIC channels and the attending structural and functional homology are make the claims drawn to a single inventive concept.

It is noted that Group I contains claim 1, which under 37 CFR 1.475(d), shall be considered as the main invention of the claims. Claim 1 reads:

> (1) Protein constituting a mammalian neuronal cationic channel that is sensitive to amiloride and activated by protons.

Furthermore, claim 2 specifically claims SEQ ID NO:1 or a functionally equivalent derivative, it is not limited to SEQ ID NO:1 alone. Functional equivalence is found in the other ASIC proteins Applicants earnestly submit that all of the claims share the special technical features:

(a) all involve neuronal channels
    (1) all are mammalian
    (2) all are cationic
(b) all involve sensitivity to amiloride
(c) all involve activation by protons

Thus all of the channels fall under Claim 1 which is generic to the neuronal cationic channels claimed in the present invention and all such claims should be classed with claim 1 in Group I..

Applicants respectfully submit that the ASICs are not structurally different, but have high homology. Furthermore, the ASICs are not functionally different as they function as proton-activated, amiloride-sensitive neuronal cationic channels. These newly discovered channels, with the accompanying technical features represent an advance over what is known in the prior art.

The products and processes embodied in the claims demonstrate unity of invention pursuant to 37 CFR 1.475(b). Moreover, it is common practice in the United States to examine nucleic acid embodiments, amino acid embodiments and methods of using proteins in a single application. Applicants, therefore, urge that there is unity of invention, and request examination of all claims.

In the alternative, we urge the Examiner to consider that there are three basic types of ASIC channels claimed: ASIC1 (Claims 1-3 and 5), ASIC2 (Claims 1 and 4) and ASIC3 (Claims 1 and 6) and these should form the basis of three Groups of claims rather than thirteen. Should the Examiner agree with the proposition of the three groups, we urge the Examiner to consider that each group should include the claims to the nucleic acid sequence for the ASIC channel, the corresponding vector, the methods of transforming cells the transformed cells, methods of using the cells for screening of compounds capable of modulating the channel activity, and the anti-channel antibodies. This would lead to the Groups of claims as follows:

Group I: Claims 1-3, 5, 10-13, 15, and 17-25

Group II: Claims 1, 4, 10-11, 14, and 17-25

Group III: Claims 1, 6, 10-11, and 16-25

Of these, the Applicants would elect Group I (Claims 1-3, 5, 10-13, 15, and 17-25).